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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/549,648	09/15/2005	Gregor Sagner	21810-US	2235

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EXAMINER	
PANDE, SUCHIRA	
ART UNIT	PAPER NUMBER
1637	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/549,648	SAGNER ET AL.	
	Examiner	Art Unit	
	SUCHIRA PANDE	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 20, 2008 has been entered.

Claim Status

2. Amendment filed on August 20, 2008 is acknowledged. Claims 1-14 are cancelled. Base claim 15 has been amended. Claims 15-17 are pending in the application and will be examined in this action.

Response to Arguments

Re rejection of claims 15-17 under 35 U.S.C. 103(a) over Bell and Ranford-Cartwright as evidenced by Wittwer et al. (1997), in view of Pinkel et al.; Epstein et al.; and Glazer et al.

3. Applicant's arguments filed August 20, 2008 have been fully considered but they are not persuasive. Applicant has amended the base claim 15 to add limitations in an effort to better define the structure of the claimed instrument. The two newly added limitation are:

(i)---- emitting light toward a reaction vessel containing fluorescent compounds.,

(ii) --- each said bundle receiving homogeneously distributed light emitted from the reaction vessel,, and transmitting said light---

Applicant is reminded that the invention under prosecution is an instrument and not a method.

The amended claims should refer to structural components that distinguish the invention disclosed in Fig. 4 of the instant application over cited art. In the present amendment both the added limitations refer to active method steps describing how the device functions and not to actual component of the device themselves. Hence in the present situation where an instrument is being prosecuted these method steps or intended use steps do not help distinguish the claimed invention over cited prior art. The added limitations refer to situations that occur when the instrument is being used. However when the claimed instrument is switched off then neither added limitation (i) or (ii) described above applies. Thus both these newly added limitations are not structural limitations that refer to actual component of the device. If the Applicant can amend the claims to capture distinguishing features of the instrument disclosed in Fig. 4 in the recited claim language in terms of the structural components and their spatial relationship to each other rather than how these components function when the instrument is being used, that would be helpful in moving the prosecution further.

Prior art teach all the structural components recited in the claim 15 as currently presented. The claims are drawn to a real time PCR instrument. The only structural features associated with the claimed instrument are

a light source;

5 optical fiber bundles;

5 separate fluorescent detector entities;

each of said detector entities having a central detection wavelength, said wavelengths being distinct from each other by at least 25 nm;

means for heating and cooling; and

multiple reaction vessels.

The cited art teaches all the above elements.

Ranford-Cartwright teaches: real time PCR instrument (see page 339 Table 1 where comparison of 7 different real time PCR thermal cyclers is done).

a light source ; Wittwer et al. teaches at least 1 light source, (See page 17 abstract where blue light-emitting diode (LED is taught).

Wittwer et al. teaches fluorescent detector having central detection wavelength, said wavelengths being distinct from each other by at least 25 nm (Wittwer et al. teaches use of different filters for detection of SYBR® Green I (520-580 nm) , fluorescein (520-550 nm), rhodamine (580-620 nm) and Cy5™ (660-680 nm) dyes (see page 177 par. 3 and page 178 par. 1). Therefore they teach detection of four dyes SYBR® Green I , fluorescein, rhodamine and Cy5™ , each of said entities having central detection wavelengths which are distinct from each other by at least 25 nm (As can be seen from the wavelengths taught above that central detection wavelengths are distinct from each other by at least 25 nm),

means for heating and cooling (See page 178 section labeled Commercial Light Cycler par. 2 where Wittwer et al. teaches heating cartridge

and a motor that drives chamber fan as a means for heating. The heater is disabled and the fan is run at high speed as cooling means).

multiple reaction vessels for containing a reaction mixture (See Fig. 2 where Wittwer et al. teaches 24 sample carousel as multiple reaction vessels for containing a reaction mixture)

5 optical fiber bundles; Pinkel teaches a plurality of at least 5 optical fiber bundles (see abstract where plurality of groups of optical fibers are taught. By teaching plurality of groups of optical fibers Pinkel et al. teach a plurality of a least 5 optical fiber bundles,.

5 separate fluorescent detector entities (Pinkel et al. teach--These fibers, or group of fibers within a bundle, may be uniquely identified so that the fibers, or group of fibers, can be discreetly addressed. Further Pinkel et al. teach --The transmission ends of the optical fibers are then discreetly addressed to detectors--such as a multiplicity of optical sensors. (see abstract)., Thus teaching each said bundle transmitting light to one of a plurality of at least 5 separate detector entities).

and each said bundle transmitting light to one of a plurality of at least 5 separate fluorescent detector entities (Pinkel et al. teach the transmission end of the optical fibers comprising the optical fiber array are addressed to permit interrogation and detection of binding events (see col. 12 lines 51-53). They go on to teach the transmission ends, may be addressed by attaching the transmission end of each optical fiber or bundle of optical fibers bearing a particular biological binding partner to an individual detector (see col. 13 lines 1-

5). i.e. they teach each said bundle transmitting light to one of a plurality of separate detector entities (see col. 13 line 9 where use of one or more detectors is taught).

Applicant is arguing prior art cited lacks a critical limitation on distinct wave length windows. Contrary to Applicant's arguments prior art cited does not lack a critical limitation on distinct wave length windows as Wittwer et al. does teach distinct wavelenght window see above. As pointed out by Examiner that Wittwer only teaches use of at least 4 filters for detection of SYBR green I, fluorescein, Rhodamine and Cy5. It would be obvious to one of ordinary skill in the art that when one is using plurality of separate (5 separate) detectors to use 5 filters with appropriate central detection window as taught by Wittwer.

Claim 17 where range of the detection wavelengths is recited has not been considered by Examiner as it refers to intended use. The claim in the present form does not recite a structural component that limits the detection wavelength to the recited ranges.

Thus contrary to Applicant's arguments prior art cited does not lack a critical limitation on distinct wave length windows as Wittwer et al. does teach distinct wavelenght window.

As a final point Applicant is arguing limitations that refer to principle of operation of a device in other words limitations that refer to the intended use. As pointed out above, Applicant's arguments regarding how Pinkel differs from the principle of operation are not being considered because the instant claims are ditected towards an instrument not a method of use.

Therefore the cited rejections are valid and are being maintained. Claims 15-17 remain rejected over cited art.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bell and Ranford-Cartwright (2002) Trends in Parasitology Vol. 18, No.8. pp-337-342 (provided by applicant in IDS) as evidenced by Wittwer et al. (1997) Biotechniques vol. 22, No.1 pp176-181, in view of Pinkel et al. (US pat. 5,837,196 issued November 17, 1998); Epstein et al. (2002) Analytica Chimica Acta 469: pp 3-36; and Glazer et al. (US pat. 6,150,107 issued Nov 21, 2000).

Regarding claim 15, Ranford-Cartwright teaches: real time PCR instrument (see page 339 Table 1 where comparison of 7 different real time PCR thermal cyclers is done. On page 339, Ranford-Cartwright teach LightCycler™ but do not recite structural details associated with this cycler. Wittwer et al. explicitly provides the structural details associated with LightCycler™ PCR instrument) comprising;

Regarding claim 15, Wittwer et al. teach at least 1 light source, preferably an LED (See page 17 abstract where blue light-emitting diode (LED is taught);

Wittwer et al. teaches use of different filters for detection of SYBR® Green I (520-580 nm) , fluorescein (520-550 nm), rhodamine (580-620 nm) and Cy5™ (660-680 nm) dyes (see page 177 par. 3 and page 178 par. 1). Therefore they teach detector entities having central detection wavelengths which are distinct from each other by at least 25 nm (As can be seen from the wavelengths taught above that central detection wavelengths are distinct from each other by at least 25 nm).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use appropriate number of filters of appropriate central detection wavelength so as to be able to detect the emission spectra of each of the dye combinations used as fluorescent labels. 2144.06 Art Recognized Equivalence for the Same Purpose [R-6]>II. < SUBSTITUTING EQUIVALENTS KNOWN FOR THE SAME PURPOSE. In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency

must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. *In re Fout*, 675 F.2d 297, 213 USPQ 532 (CCPA 1982).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to make an instrument that had filters designed to filter out 5 different emission spectra instead of just 4 emission spectra taught by Wittwer et al. An ordinary practitioner would have recognized that the results optimizable variables of different number of fluorescent dye combinations that can be used or adjusted to maximize the desired results. As noted in *In re Aller*, 105 USPQ 233 at 235,

> More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Routine optimization is not considered inventive and no evidence has been presented that the selection of 5 different wavelengths was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

Regarding claim 15, Wittwer et al. do not teach the limitation:

•a plurality of a least 5 optical fiber bundles, each said bundle transmitting light to one of a plurality of at least 5 separate fluorescent detector entities,

Regarding claim 15, Pinkel et al. teach : a plurality of a least 5 optical fiber bundles, (see abstract where plurality of groups of optical fibers are taught. By teaching plurality of groups of optical fibers Pinkel et al. teach a plurality of a least 5 optical fiber bundles,.

each said bundle transmitting light to one of a plurality of at least 5 separate fluorescent detector entities (Pinkel et al. also teach--These fibers, or group of fibers within a bundle, may be uniquely identified so that the fibers, or group of fibers, can be discreetly addressed. Further Pinkel et al. teach --The transmission ends of the optical fibers are then discreetly addressed to detectors--such as a multiplicity of optical sensors. (see abstract)., Thus teaching each said bundle transmitting light to one of a plurality of at least 5 separate detector entities.

Pinkel et al. teach the transmission end of the optical fibers comprising the optical fiber array are addressed to permit interrogation and detection of binding events (see col. 12 lines 51-53). They go on to teach the transmission ends, may be addressed by attaching the transmission end of each optical fiber or bundle of optical fibers bearing a particular biological binding partner to an individual detector (see col. 13 lines 1-5). i.e. they teach each said bundle transmitting light to one of a plurality of separate detector entities (see col. 13 line 9 where use of one or more detectors is taught).

In col. 15 lines 44-48, Pinkel et al. teach fluorescent labels and in col. 16 lines 6-10 they teach how sensitivity of fluorescence detection for different

combinations of optical fiber, fluorochrome, excitation and emission bands can be optimized. Thus teaching each said bundle transmitting light to one of a plurality of at least 5 separate fluorescent detector entities

and characterized in that said plurality of detector entities is capable of simultaneously detecting maximum fluorescence emission of at least 5 different fluorescent compounds

simultaneously detecting maximum fluorescence emission of at least 2 differently labeled TaqMan hybridization probes (see Ranford-Cartwright page 338 par. labeled "Hydrolysis probes" where TAMRA and ROX labeled TaqMan hybridization probes are taught. Therefore Ranford-Cartwright teach detecting maximum fluorescence emission of at least 2 differently labeled TaqMan hybridization probes. In other words once the maximum fluorescence wavelength of these hybridization probes is known, then the fiber detectors taught by Pinkel et al. will be able to detect them) , and

detecting maximum fluorescence emission of SYBR® Green I (see Ranford-Cartwright page 338, par. labeled "Detection systems for quantification" where SYBR® Green I detection is taught. Therefore maximum fluorescence emission of SYBR® Green I is known and hence one of the fiber optic bundles taught by Pinkel et al. could be optimized to detect maximum fluorescence emission of SYBR® Green I .

Examiner would like to point out that all of the capabilities "detecting 5 different fluorescent compounds----TaqMan hyb-----, detecting fluorescence of SybrGreen I" recited above for the detector entities are only intended use and do

not impart any structural limitation to the detectors claimed. If the multiple detectors taught are capable of detecting the fluorescence then as far as the instrument is concerned it does not matter how the fluorescence was generated in the sample to be detected. All it matters is the emission wavelength window for which each of the fiber optic detectors is configured to detect.

means for heating and cooling (See page 178 section labeled Commercial Light Cycler par. 2 where Wittwer et al. teaches heating cartridge and a motor that drives chamber fan as a means for heating. The heater is disabled and the fan is run at high speed as cooling means).

multiple reaction vessels for containing a reaction mixture (See Fig. 2 where Wittwer et al. teaches 24 sample carousel as multiple reaction vessels for containing a reaction mixture)

Regarding claim 16, Wittwer et al teaches a PCR instrument comprising exactly one light source (see claim 15 above where Blue light LED source is taught).

Claim 17, recites an instrument according to claim 15-16, characterized in that said central detection wavelengths are selected from a group of range of wavelengths, said group consisting of 520-540 nm, 545-565 nm, 570-590 nm, 600-620 nm, 630-650 nm, 660-680 nm, and 700-720 nm. The range of wavelengths recited only indicate intended use and do not provide further structural limitation to the claimed instrument and hence are not being considered further.

It would have been prima facie obvious to one of ordinary skill in the art to combine a plurality of optical fiber bundles, each said bundle transmitting light to one of a plurality of separate fluorescent detector entities as taught by Pinkel et al. in the fluorescent thermocyclers taught by Ranford-Cartwright as evidenced by Wittwer et al. at the time the invention was made.

The motivation to do so is provided to one of ordinary skill in the art by teachings of Epstein et al. and Pinkel et al.

Epstein et al. while reviewing fluorescence –based nucleic acid detection and microarrays state "The Taqman assay is a solution based FRET method designed to perform quantitative PCR product measurements in real time. By monitoring the reaction progress with FRET techniques, the need for gel electrophoresis or repetitive sample handling can be avoided"-----(see Epstein et al. page 7 section 2.3.3 Taqman real time PCR detection). They go on to state "Fluorescence measurements are made directly during the ongoing PCR cycles rather than at reaction completion. Taqman allows the reaction progress to be monitored in real time and is sensitive to single nucleotide polymorphisms" (see Epstein et al. page 9, par. 1).

Pinkel et al. state "the inclusion of fibers bearing biological binding partners specific for various analytes known to create a background signal in a particular assay provides a means for simultaneously measuring and substracting out the background signal." (see col 1 lines 64-67 and col. 2 lines 1-5). Thus one of ordinary skill in the art has a reasonable expectation of success of making a fiber optics based PCR instrument where use of optical fibers to

conduct the fluorescent emission signals from the sample to detector will help filter out the background signal. This property of optical fibers will result in improving accuracy of simultaneous measurements of the various labeled products made in real time.

Glazer et al. provides information to one of ordinary skill regarding the various labels that can be used for FRET and the emission wavelengths that are used for their detection. Thus providing guidance regarding what wavelength filters to use for each individual fluorescent detector so that depending on the combination of fluorescent labels that are used and the expected maximum emission wavelengths the multiple detectors will simultaneously detect fluorescence from appropriate fluorescent dye emissions. (See whole patent specially see col. 15 lines 24-42 and Fig. 4).

Conclusion

7. All claims under consideration 15-17 are rejected over prior art.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUCHIRA PANDE whose telephone number is (571)272-9052. The examiner can normally be reached on 8:30 am -5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kenneth R Horlick/
Primary Examiner, Art Unit 1637

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